No. 2022-1258, 2022-1307 (consolidated)

United States Court of Appeals for the Federal Circuit

JANSSEN PHARMACEUTICALS, INC. AND
JANSSEN PHARMACEUTICA NV
Plaintiffs-Appellees,

v.

TEVA PHARMACEUTICALS USA, INC. AND
MYLAN LABORATORIES LIMITED
Defendants-Appellants.

Appeals from the U.S. District Court for the District of New Jersey,
Case Nos. 2:18-CV-734-CCC-LDW and 2:19-CV-16484-CCC-LDW

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INTRODUCTION

The district court decision skews the obviousness comparison from both ends: it adds unwritten limitations to the claims, and it subtracts the skilled artisan's perspective from the prior art. Each error is reversible on its own. Their combined effect is a judgment permitting Janssen to suppress competition and extract millions of dollars *per day* from schizophrenic patients, *through 2031*, with claims that recycle elements from Janssen's expired patents and old publications on the compound Janssen patented in 1993.

Rather than defending the district court's errors directly, Janssen tries to recast them as the court merely "crediting" Janssen's witnesses who urged those errors. But the court was not "simply rejecting the theory of motivation offered by Teva's expert" when it required Teva to prove obviousness of unwritten limitations. JanssenBr.2. The court's analysis—which the opening brief discussed at length—was explicitly broader than that. Nor did the court merely "credit" Janssen's expert when it limited prior art to its explicit teachings. JanssenBr.2-3. Courts do not insulate legal errors from review by "crediting" testimony urging those errors. *See, e.g.*, *Anderson v. Bessemer City*, 470 U.S. 564, 575 (1985)

(trial court cannot "insulate [its] findings from review by denominating them credibility determinations"); *Lazare Kaplan Int'l, Inc. v. Photoscribe Techs., Inc.*, 628 F.3d 1359, 1381 (Fed. Cir. 2010) (similar).

At bottom, there is no dispute that prior art already discloses administering the same doses, of the same drug, at the same intervals, to the same patients, into the same muscles, in the same form, as the claims. The claims recite those old elements and tweak known parameters in conventional ways: they specify shoulder-site injections, and unequal loading doses. The shoulder is one of three standard, obvious-to-try injection sites, and already in paliperidone-specific prior art. And the claimed loading doses are within narrow prior-art ranges and thus presumptively obvious. On the undisputed facts, the '906 patent is obvious because it merely "unites old elements with no change in their respective functions." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

Janssen's indefiniteness arguments are no better. Janssen largely ignores post-*Nautilus* precedent, in favor of an earlier decision, *Takeda Pharm. Co. v. Zydus Pharms. USA, Inc.*, 743 F.3d 1359 (Fed. Cir. 2014), that merely reaches a different result on different facts. The principle of all those cases, including *Takeda*, renders Janssen's claims indefinite.

Janssen's claims recite numerical properties that can be derived by different methods, but different methods lead to meaningfully different results, and the intrinsic evidence gives no guidance which method to use.

ARGUMENT

I. The Non-Obviousness Judgment (All Claims) Should Be Reversed or Vacated.

Obviousness compares the claims to prior art. The district court erroneously added unwritten limitations to the claims and subtracted the skilled artisan's perspective from prior art. Each error exacerbates the other. For either reason or both, the judgment must be reversed.

A. The District Court Erroneously Required Proof of Obviousness of Unwritten Claim Limitations.

1. The District Court Added Unwritten "Generalized" Safety and Efficacy Limitations to All Claims.

The district court erroneously treated all claims as reciting "*generalized*" dosing regimens that were safe and effective for a majority of patients, and required Teva to prove the obviousness of *those* reimagined claims. OpeningBr.23-29, 40-45. That is reversible error. *E.g.*, *Canfield Sci., Inc. v. Melanoscan, LLC*, 987 F.3d 1375, 1382 (Fed. Cir. 2021); *Senju Pharm. Co. v. Lupin Ltd.*, 780 F.3d 1337, 1347 (Fed. Cir. 2015); *MobileMedia Ideas, LLC v. Apple Inc.*, 780 F.3d 1159, 1172 (Fed. Cir. 2015);

Allergan, Inc. v. Apotex Inc., 754 F.3d 952, 962-63 (Fed. Cir. 2014); *Allergan Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013). Janssen's contrary arguments are unsound.

a. Janssen tries to sow confusion by noting that Teva's counsel and witnesses sometimes used "general" to distinguish between the claims that did (claims 8, 11, and dependents) and did not (claims 1, 4, and dependents) recite that the "patient" was renally-impaired. JanssenBr.33-34; *see* OpeningBr.19-22 (describing claims); Appx10201-10202(201:10-202:1) (testimony using "general" as shorthand for non-renal-impairment claims); Appx10325-10326(325:18-326:3) (same).

That is true but irrelevant. Nowhere does the district court use "*generalized*" to distinguish the renal-impairment claims. *E.g.*, Appx79 ("individualized, rather than generalized, dosing"); OpeningBr.42-43. And the problem is not that a word appears in the opinion. It is that the court adopted *Janssen's arguments* to treat the claims as limited to "*generalized*" dosing regimens, safe and effective for most patients, and to require Teva to prove obviousness of those reimagined claims. OpeningBr.23-29, 40-45.

Janssen's strategy to narrow the claims began at opening statements. Teva anticipated "[y]ou're likely going to hear from Janssen that [Invega Sustenna] is special because it can be used for any patient, can treat all patients," but reminded the court "the claims are limited to a dosing regimen for treating a patient, only one," and Teva's burden of proof concerned the claims as written. Appx10018-10019(18:20-19:25). As predicted, Janssen's opening statement contended it "develop[ed] a dosing regimen that would apply to an entire patient population." Appx10047(47:4-5). "*And this is really important*," Janssen added, "[t]he regimen *has to work for everyone*." Appx10047(47:5-7).

When Teva asked witnesses to confirm that the claims did not require efficacy or any number of patients, Janssen objected. *E.g.*, Appx11423-11424(1423:5-1424:11). Janssen witnesses resisted those questions, insisting that the *claims* required unwritten efficacy results for broad patient populations:

> [Teva's counsel]: *[T]he claim* doesn't require any particular number of patients, right?
>
> [Janssen's witness Samtani]: *But the claim came from* calculations that ensure that *a vast majority of subjects get into therapeutic concentration range,* and *that is what led to claims like these.*

> [Teva's counsel]: It doesn't say "vast number of patients," right?
>
> [Samtani]: Yeah, it does not use those exact words.

Appx11424(1424:13-19); *e.g.*, Appx11424-11425(1424:20-1425:22) (Samtani, similar); Appx11657-11658(1657:2-1658:3) (Janssen expert Sinko, arguing claims required "rapid efficacy and long-term efficacy"); Appx12540-12541(2594:22-2595:12) (Janssen expert Mulhern, similar).

Janssen continued that strategy in closing arguments, Appx13011-13012(100:15-101:10), and post-trial briefs, including characterizing regimens as "failures" if they were safe and effective for less than a generalized patient population, and faulting Teva for purportedly failing to prove obviousness of such "generalized" regimens. *See* Appx1150; Appx1167; Appx1169; Appx1187; Appx1247; Appx1254; Appx1271-1272; Appx1279-1280; Appx1289; Appx1358; Appx1690; Appx1692 n.15; Appx1697.

Contrary to Janssen's suggestion, Teva never agreed to or invited Janssen's view of the claims. Teva's experts consistently testified that the claims only recited treating *a patient*, Appx10200(200:12-16); Appx10205(205:4-13); Appx10319(319:17-23); Appx10325(325:6-11), and Teva's post-trial briefs emphasized that the claims had that scope. *E.g.*, Appx1431-1432; Appx1422 n.5; Appx1435; Appx1445; Appx1559;

Appx1618-1619; Appx1856-1857; Appx1859; Appx1865. After all of this, however, the district court adopted Janssen's arguments for reading in unwritten limitations. OpeningBr.23-29, 40-45.

b. Janssen contends the district court's discussion of "generalized" regimens was limited to evaluating Teva's motivation-to-combine argument. JanssenBr.35-36. It was not. *See* OpeningBr.41-45. The court declared that the patent "*claims* a *generalized* dosing regimen," Appx78, distinguished prior art as teaching "individualized, rather than generalized dosing," Appx79, and lacking clinical data that would make a "generalized" regimen obvious. Appx71-74; Appx88; Appx91-92 & n.34. The court found *reasonable expectation of success* lacking because "developing a *generalized* multi-dose regimen using an LAI to initiate therapy" was unpredictable. Appx87. "[T]o successfully arrive at a multi-dose regimen based on the prior art," the court opined, "a POSA *would need safety, efficacy, and pharmacokinetic data* in order to evaluate how a *generalized* dosing regimen would perform *in patients*." Appx88.

The court's analysis is thus explicitly broader than motivation-to-combine, and commits the "legal error" of "[f]ail[ing] to consider the ap-

propriate scope of the patent's *claimed invention* in evaluating the reasonable expectation of success." *Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (quoting *Allergan v. Apotex*, 754 F.3d at 966); *see also Dr. Falk Pharma GmbH v. GeneriCo, LLC*, 774 F.App'x 665, 675-76 (Fed. Cir. 2019).

Janssen emphasizes the claims' "*purpose* of treating patients," and argues that *Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331, 1340-43 (Fed. Cir. 2021); *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381-82 (Fed. Cir. 2021); and *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1383 (Fed. Cir. 2019) support the district court's use of unclaimed safety and efficacy properties in connection with reasonable expectation of success. JanssenBr.38-39. Those decisions only underscore the district court's error. In all three, the *claims* required safety or efficacy. *Eli Lilly*, 8 F.4th at 1335 ("an *effective* amount" of an antibody); *OSI*, 939 F.3d at 1378-79 ("a *therapeutically effective* amount"); *Corcept*, 18 F.4th at 1381 (as construed by the PTAB, "claim 1 … requires safe administration of a specific amount of mifepristone").

Janssen's claims, however, do not require safety, efficacy, or other results. Nor could they, as the written description discloses no such results for the claimed regimens. Janssen's claims only require a dosing regimen comprising administering an LAI paliperidone formulation to *a* patient. To be sure, the claimed patient is "in need of treatment," but that is *who receives* the drug, not what effect the drug has. *See* Appx11693(1693:9-19) (Janssen's expert Sinko: "a patient whose treatment did not succeed would still, you know, meet this claim"). It was thus error to require Teva to prove a POSA would have expected such results. *See Allergan v. Apotex*, 754 F.3d at 966; *Intelligent Bio-Systems*, 821 F.3d at 1367; *BTG Int'l Ltd. v. Amneal Pharms. LLC*, 923 F.3d 1063, 1075 (Fed. Cir. 2019).

c. The district court opined "a POSA would need *safety, efficacy, and pharmacokinetic data* in order to evaluate how a *generalized* dosing regimen would *perform* in patients," Appx88, and faulted prior art for lacking such data. Appx71-74. Again, the claims do not require safety, efficacy, or any performance in patients. Requiring such data from the prior art further confirms that the court read unwritten limitations into the claims. That is not to say that presence or absence of prior-art clinical

data is irrelevant, JanssenBr.41-42, only that requiring such data is inconsistent with the claims' scope.

Janssen defends that discussion by citing cases where, again, the patents actually *claimed* efficacy. JanssenBr.40 (citing *Eli Lilly* and *OSI*, discussed *supra* p.8, and *Novartis Pharms. Corp. v. West-Ward Pharms. Int'l Ltd.*, 923 F.3d 1051, 1054 (Fed. Cir. 2019), where claims recited "administering…a therapeutically effective amount"). Janssen's claims have no such requirements, nor could they.

Janssen contends that the absence of prior-art clinical data supports the finding of no reasonable expectation of success. JanssenBr.39. But that finding and the significance the district court ascribed to it are tainted by the same legal error explained above—there is no claim limitation dictating a particular result of drug administration. Moreover, Janssen understates the record evidence. Janssen ignores, for example, that the prior-art '548 protocol is a *Phase III* study, which is by definition premised on a reasonable expectation of safety and efficacy. *See* OpeningBr.15. FDA regulations define Phase III studies as "performed after preliminary *evidence suggesting effectiveness … has been obtained*," and "intended to gather the *additional* information about effectiveness and

safety." 21 C.F.R. §312.21(c). One of the '906 patent's inventors, Gopal, admitted he *expected* the '548 protocol to meet safety and efficacy end-points. Appx11123-11124(1123:13-1124:20); *see also* Appx10758(758:6-25) (Inventor Vermeulen describing Phase III as confirming "both the safety" and "expected efficacy").

Janssen argues that a POSA would not expect success for regimens that "went against the 'traditional dosing paradigm' of starting low and going slow." JanssenBr.42-43. But the prior-art '548 protocol describes administering doses up to 150 mg-eq. of paliperidone palmitate on days 1, 8, 36, and 64, which is *higher* than the claimed doses, not low or slow.

Finally, Janssen own "unexpected setbacks" is makeweight and un-responsive. JanssenBr.43 (citing Appx88-89, and *Endo Pharms. Inc. v. Actavis LLC*, 922 F.3d 1365, 1377 (Fed. Cir. 2019)). *Endo* is, again, a case where the salient evidence was actually connected to the claims. The *Endo* claims required specific purity levels, and the inventors' failure to achieve those levels was relevant. 922 F.3d at 1377. Janssen's claims have no similar limitations, and Janssen's "setbacks" showed efficacy in low-BMI patients, in any event. Appx11146-11147(1146:2-1147:9).

2. The District Court Added an Unwritten "Mild" Limitation to the Renal-Impairment Claims.

The district court's error of adding a "mild" limitation to the renal-impairment claims is not complicated. Claims 8, 11, and dependents all recite "administering paliperidone palmitate to a *renally impaired* psychiatric patient." Appx174-175. The court declared that "the '906 Patent 'focuses on *mild* renal impairment,'" Appx82, and distinguished prior art specifically because it did not specify *mild* renal impairment. Appx82-83. Janssen does not dispute that the claims lack any "mild" renal impairment limitation. That should be the end of the matter.

The district court did not, as Janssen contends, simply reject an expert's motivation-to-combine theory. JanssenBr.53-55. The court said outright: the claimed "dosing regimens address patients *with mild renal impairment*, and neither the '591 application nor Cleton 2007 *expressly teach* LAI paliperidone palmitate dose reductions *for mild renal impairment*." Appx82-83. Cleton 2007 expressly discusses renal impairment. Appx14112. The '591 application discusses liver impairment, Appx16292-16293, and explains that paliperidone is cleared through the kidneys. Appx16297(¶39).

Janssen quotes Wermeling referring to "mild" impairment, but omits context. JanssenBr.53. The context was a line of questioning about the prior-art Invega ER label. Wermeling testified, accurately, that the label states the maximum dose for a patient with healthy kidneys is twice the dose for a patient with mild renal impairment. Appx10332(332:1-15). That testimony was not some broad concession that the *claims* were limited to mild renal impairment or that prior art discussing renal impairment generally was irrelevant. Indeed, the same testimony discussed Cleton 2007 on the preceding page. Appx10330-10331(330:19-331:14).

B. The District Court Erroneously Limited the Prior Art to Explicit Disclosures.

Prior art specific to paliperidone palmitate disclosed the exact claimed formulation, loading doses, and maintenance doses for intramuscular injection. *See* OpeningBr.36. The only claim element not expressly taught in *paliperidone-specific* prior art is the "unequal" loading doses. *But see* OpeningBr.26-27 (prior art taught unequal loading doses of antipsychotics); Appx78-79. The unequal loading doses are **(1)** presumptively obvious because they are within narrow prior-art ranges, and **(2)** not shown to be critical to the claims. Although Janssen refers several times to having "perfected" or "selected" doses, Janssen merely "selected" from

among numerous regimens that were *all* expected to work. *See* OpeningBr.61-62; Appx170(23:26-24:26); Appx174(31:30-49). Indeed, inventors testified that other regimens, such as 100/100 mg-eq., worked equally well for most patients and that Janssen told the FDA as much. Appx10893-10896; Appx10912; Appx11359; Appx11426-11427; Appx10919; Appx11181-11182.[1]

The court also dismissed "the three primary prior art references" because none "teach[es] deltoid administration of *loading doses*." Appx74-75. It is undisputed, however, that the deltoid is one of three standard injection sites, and paliperidone prior art taught deltoid injections. Appx16204; Appx16206. Prior-art textbooks taught the advantages and disadvantages of all three injection sites, but the court dismissed them because "neither discloses deltoid administration *of LAI loading doses*." Appx75-76. Prior art from the 1990s taught loading doses of LAI antipsychotics, but the court dismissed those references for

[1] For at least two studies that Janssen called "failures" in this litigation (using unclaimed regimens), the Invega Sustenna label lists the studies and states they were "superior to placebo." *See* Appx13130(§14); Appx11133(1133:10-19) (PSY-3004 study Janssen called "failure" and "disaster" is on the label); Appx11129-11130(1129:9-1130:23) (PSY-3003 study Janssen called "failure" is on the label showing efficacy for 100/100 loading doses).

not using paliperidone specifically. Appx78-79. That is not how obviousness works.

Had the district court considered the prior art "not only for what it expressly teaches, but also for what it fairly suggests" to a skilled artisan, it would have concluded the claims are obvious. *Bradium Techs., LLC v. Iancu*, 923 F.3d 1032, 1049 (Fed. Cir. 2019). Instead, as in cases like *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1076-77 (Fed. Cir. 2015), and *Duramed Pharms., Inc. v. Watson Lab'ys, Inc.*, 413 F.App'x 289, 294-95 (Fed. Cir. 2011), the court considered each reference in isolation, limited it to its explicit teachings, and essentially held that the '906 patent's claims were not obvious because no single reference anticipated. In other words, as in *Duramed*, "the district court erred in assessing the content and scope of the prior art, leading it to incorrectly analyze each prior art reference in isolation without considering the prior art['s] teaching as a whole in light of the creativity and common sense of a person of ordinary skill." 413 F.App'x at 294; *see also, e.g.*, *KSR*, 550 U.S. at 415, 419 (reversing nonobviousness judgment); *E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1011 (Fed. Cir. 2018) (same); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1368 (Fed. Cir. 2007) (same).

1. Janssen's "Credibility" Framing is Inapt.

Janssen's main response is to change the subject. Janssen reframes the district court's errors as "credibility" judgments warranting deference. JanssenBr.45-46. Janssen's brief refers at least 36 times to the district court having "credited" or found "credible" some aspect of Janssen's argument. But legal errors cannot be shielded from review by labeling them "credibility determinations" or purporting to credit testimony founded on legal error. *E.g., Anderson*, 470 U.S. at 575 (trial court cannot "insulate [its] findings from review by denominating them credibility determinations"); *Lazare*, 628 F.3d at 1381 (similar, quoting *Andreu v. Sec'y of HHS*, 569 F.3d 1367, 1379 (Fed. Cir. 2009)). The district court's errors are as reversible here as the reviewed tribunals' errors in *Belden*, *Duramed*, *Dupont,* and *Pfizer*.

Janssen contends the "primary reason" for the nonobviousness ruling was that Janssen's expert "'credibly testified' that *nothing* in the prior art or a POSA's knowledge would teach that the 548 protocol *needed to be modified*, or, if so, how." JanssenBr.44-45. A patentee cannot avoid obviousness by arguing individual prior-art references are somehow

"good enough" that no skilled artisan would modify them. Precedent recognizes the "normal desire of scientists or artisans to improve upon what is already generally known…." *See DuPont*, 904 F.3d at 1011; *see also In re Ethicon, Inc.*, 844 F.3d 1344, 1351 (Fed. Cir. 2017) (similar); *Pfizer*, 480 F.3d at 1368 (similar). The '548 protocol taught administering buttock injections of paliperidone palmitate at the same intervals, and in amounts (50-150 mg-eq.) overlapping the claimed doses. Appx13244-45. *See* OpeningBr.36 (chart). Variations on injection sites and doses were well-explored in prior art generally, and in paliperidone-specific prior art. The notion that a skilled artisan would do *nothing* with the '548 protocol is contrary to precedent and cannot be dismissed as a "credibility" finding.

2. Janssen's Defenses of Individual Distinctions are Unsound.

a. Shoulder injections (all claims). Janssen defends the district court's discussion of shoulder-site claim limitations by arguing buttock injections were generally preferred for LAI antipsychotics because that site involves less pain than other sites. JanssenBr.47-49.[2] That is

[2] The Wermeling testimony Janssen cites does not "disavow[] … routine optimization." JanssenBr.48. It explains only that each drug goes

irrelevant. Janssen does not dispute that the shoulder was one of three standard injection sites, whose relative pros and cons were well-known. Relative pain levels were merely a known trade-off. Many patients preferred buttock injections for pain reasons. Many others, particularly "in the United States," undisputedly preferred *not* to have buttock injections because they prioritized privacy. Appx77-78 (quoting Gopal testimony at Appx11180-11181(1180:20-1181:2)). Appx10857(857:12-20) (inventor Vermeullen agreeing "privacy concerns" led some patients to prefer shoulder injections over buttock injections); Appx11911-11912(1911:23-1912:7); Appx11960(1960:6-10) (Janssen expert Kohler, similar, agreeing such "privacy concerns … existed before 2007"); Appx12311(2311:6-21) (Teva expert Kahn, similar). In any event, Janssen does not dispute that its own trials, also prior art, injected paliperidone palmitate into the shoulder. OpeningBr.17-18 (citing Appx16204; Appx16206).

Janssen undisputedly did not invent shoulder injections, discover some unexpected benefit of shoulder injections, or discover a way to make

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through the same general development process. Appx10363(363:2-8); Appx10364(364:3-24).

shoulder injections less painful—either generally or for paliperidone palmitate specifically. All Janssen did was to select from among a "finite number [three] of identified, predictable solutions." *KSR*, 550 U.S. at 421. It took advantage of the fact that no single prior-art reference disclosed shoulder injections combined with unequal doses (*i.e.*, no reference anticipated), to extend its exclusivity by mixing those known variables. Precedent requires consideration of prior art for all it teaches, and cannot be waved away with the "credibility" label. The district court erroneously limits each prior-art reference to its expressly-recited injection sites. Appx74-76; Appx69 n.20. That is legal error.

b. Unequal loading doses (all but the renal-impairment claims). Janssen's defense of the "unequal loading doses" distinction largely repeats the district court's errors. JanssenBr.49-50. Janssen refers to its claims as a "unique combination of elements," JanssenBr.49, but does not dispute that the '548 protocol taught paliperidone palmitate injections at the same claimed intervals and in amounts (50-150 mg-eq.) overlapping the claimed doses. Appx13244-45. Nor does it dispute that WO'384 taught the exact Invega Sustenna formulation in syringes for administration in amounts from 25-150 mg-eq, exactly matching the

range of claimed doses.[3] Appx13316-13317; Appx12162(2162:2-7); Appx12163(2163:15-20); s*ee* OpeningBr.36 (chart). Nor does Janssen argue that it invented unequal loading doses or that the claimed doses had some unexpected advantage vis-à-vis the rest of the prior-art ranges.

Janssen's claims are only a "unique combination" in the banal sense that this is not an anticipation case. Where, as here, "prior art as a whole … taught" the claimed regimen and "conditions either identical to or overlapping with" the claims, the claims are presumptively obvious. *DuPont*, 904 F.3d at 1011.[4] Janssen cites nothing to rebut the presumption. Here, prior art already taught doses between 25-150 mg-eq. administered at the same intervals. Choosing a 100 mg-eq. dose for day 8 was

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[3] WO'384's Example 4 is "Preparation of finished form." Appx13316. Janssen is thus wrong to suggest WO'384 "discloses the final formulation only in passing." JanssenBr.25 n.5. Nor is it true that WO'384 has "no information about particle size." *Id.* WO'384 discloses "[m]ost preferably, essentially all of the particles have a size of less than 2,000 nm." Appx13306-13307; Appx13240(5:24-25).

[4] *See also, e.g.*, *In re Applied Materials, Inc.*, 692 F.3d 1289, 1298 (Fed. Cir. 2012) ("that multiple [prior-art] variables were combined does not necessarily render their combination beyond the capability of a person having ordinary skill in the art"); *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004) (whether an element was "disclosed within a single patent" or "in multiple prior art patents" was "a distinction without a difference"); *Valeant Pharms. Int'l, Inc. v. Mylan Pharms. Inc.*, 955 F.3d 25, 31-32 (Fed. Cir. 2020) (similar).

routine tinkering within disclosed ranges. Only by erroneously limiting prior art to its express disclosures—such as dismissing Ereshefsky for discussing different drugs, or dismissing the '548 protocol for using equal loading doses—could the district court uphold these claims.

c. Reduced doses of a renally-metabolized drug for renally-impaired patients (claims 8, 11, and dependents). Janssen barely responds to Defendants' showing of error with respect to the renal-impairment claims, *compare* OpeningBr.53-56, *with* JanssenBr.54-55, except to argue that "[t]o the extent" Teva's obviousness theories "started from claim 2," the district court did not err by noting that the loading doses of renal-impairment claims were not precisely half the loading doses of other claims. JanssenBr.54-55.

Teva's arguments were based on prior art, not other claims. OpeningBr.54-55. As Teva argued below and Janssen ignores, the claimed doses were within prior-art ranges and thus presumptively obvious. Appx1437; *see, e.g.*, *DuPont*, 904 F.3d at 1011; *cases cited supra* p.20 n.4. More fundamentally, Janssen does not dispute that it was well-known that the kidneys metabolize paliperidone palmitate, and that patients with impaired kidneys should be given lower doses of kidney-metabolized

drugs. As Teva argued, and Janssen ignores, the Invega ER (paliperidone palmitate) and Risperdal (paliperidone precursor) labels—both prior art—advise half-doses for renally-impaired patients. *See* OpeningBr.18; Appx1438-1439. The district court upheld the renal-impairment claims by erroneously limiting those references to their explicit disclosures, dismissing them because they taught a different drug or a different form of the same drug. Appx81-83.

d. Particle size (claims 19-21). Janssen does not dispute that the '544 patent and WO'384 disclose a preferred paliperidone palmitate particle size of less than 2000nm, which encompasses the claimed 900-1600nm range. Nor does Janssen dispute that particle size is a *result-effective variable* that those references taught how to control. *See* OpeningBr.56-57; JanssenBr.9, 51. That should be the end of the matter as it is obvious to modulate known result-effective variables. *See Applied Materials*, 692 F.3d at 1295; *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980).

AstraZeneca AB v. Mylan Pharms. Inc., 19 F.4th 1325, 1336 (Fed. Cir. 2021), which Janssen cites, JanssenBr.51-52, is inapposite. The Court in *AstraZeneca* observed that although prior art taught two formulations, there was expert testimony that the specific prior-art values

"were not suitable" and "clearly don't work." 19 F.4th at 1336. The claimed particle sizes were also *different* from prior art and the prior-art sizes were unsuitable for inhalation. *Id.* at 1337. There is nothing similar here. The claimed and prior-art particle sizes overlap.

Janssen otherwise relies on a common misstatement of "teaching away." Janssen argues the '544 patent taught away from the claimed particle size because one example in that patent's disclosure that was within the claimed particle size was not among those selected for further investigation. JanssenBr.51-52. As a matter of law, that is not "teaching away," as "teaching that a composition may be optimal or standard does not criticize, discredit, or otherwise discourage investigation into other compositions." *Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 738-39 (Fed. Cir. 2013). Janssen ignores, moreover, that the '544 patent expressly teaches "[m]ost preferably, essentially all of the particles have a size of less than 2,000 nm." Appx13240(5:24-25). "Less than 2,000 nm" includes the claimed particle size. That teaching cannot be dismissed because prior art also discloses other things, Appx84-86, nor ignored because the district court "credited" expert testimony that ignored it. JanssenBr.51-52.

C. Secondary Considerations Do Not Prevent Reversal or Vacatur.

1. Janssen Appears Not to Dispute that this Court Need Not Reach Secondary Considerations to Reverse or Vacate the Judgment.

The nonobviousness judgment must be reversed for either or both errors of adding unwritten limitations to the claims and limiting prior art to express teachings. Secondary considerations do not change that result, as secondary considerations "without invention will not make patentability." *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 283 (1976).

Janssen does not dispute that the district court's opinion does not assign any particular weight to the secondary-considerations evidence. The court did not find secondary-considerations evidence "strong," independently sufficient to support the judgment, dispositive; it merely stated that it considered the evidence and that various categories favored Janssen. *See* OpeningBr.29-30, 58-59. Janssen argues secondary-considerations evidence was "integral" to the judgment, JanssenBr.56, but Janssen apparently means only that the court considered the evidence as *part of* the obviousness analysis. That is true, but irrelevant. Janssen appears not to dispute that this Court can reverse or vacate the judgment without reaching secondary considerations. *E.g.*, *Ohio Willow Wood v.*

Alps S. LLC, 735 F.3d 1333, 1344 (Fed. Cir. 2013); *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1245-46 (Fed. Cir. 2010). The Court thus need go no further to address obviousness. If it does, Janssen's secondary-considerations arguments are unsound.

2. Janssen's Secondary-Considerations Arguments Repeat the District Court's Errors.

a. "Unexpected results" must be **(1)** different in *kind* and not merely degree, **(2)** unexpected compared to the closest prior art, and **(3)** unexpected from the perspective of a skilled artisan. *Galderma*, 737 F.3d at 739; *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 969-70 (Fed. Cir. 2006); OpeningBr.60-66.

Janssen all but admits its "unexpected results" were of degree rather than kind. JanssenBr.62-63. Janssen does not dispute that the Invega Sustenna formulation, dosing intervals, and dosing amount ranges were in the prior art or that it expected success in its Phase III trials. It instead argues that "rapid efficacy for the *vast majority* of subjects" set the claimed dosing regimens apart. JanssenBr.62. Janssen's "vast majority" hedge implies that at least some patients achieved the same rapid efficacy with prior-art regimens. Janssen similarly hedges when describing the allegedly failed trial under the '548 protocol as not having

"show[n] any efficacy *for most doses*." JanssenBr.62. But more than the hedging in its brief, Janssen's own cited inventor testimony confirms that the "unexpected results" were of degree rather than kind: *73%* of patients achieved the target by day 8 with the prior-art 100/100 mg-eq. regimen, compared with *84%* for the 150/100 mg-eq regimen. JanssenBr.62 (citing Appx11105-11106(1105:10-1106:9)); *see also* Appx11205-11206(1205:3-1206:14) (Gopal testifying a *higher percentage* of patients reach desired blood levels with the claimed regimen versus the other regimens). Those are differences in degree, not kind. *Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1334-35 (Fed. Cir. 2014) (affirming summary judgment of obviousness); *Galderma*, 737 F.3d at 739.

The distinction between degree and kind also distinguishes Janssen's case citations. JanssenBr.62. In *Leo Pharmaceutical Products, Ltd. v. Rea*, 726 F.3d 1346 (Fed. Cir. 2013), the inventors submitted actual test results showing a difference in kind over prior art. *Id.* at 1358. In *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293 (Fed. Cir. 2015), there were two unexpected results: **(1)** the prior art expressly taught that including the claimed ingredient in the formulation would either have no

impact on or would decrease drug permeability, but it unexpectedly *increased* it; and **(2)** the prior art taught reducing the drug content would "significantly reduce[] efficacy" without reducing side effects. *Id.* at 1306-07. Here, the identical formulation was in prior art and Janssen's modeled results showed efficacy for the prior-art regimens. *See, e.g.*, Appx13316-13317; Appx12162(2162:2-7); Appx12163(2163:15-20); Appx11105-11106(1105:10-1106:9). Janssen's preference for a higher percentage of patients reaching a target cannot convert that difference in degree to a difference in kind.

Contrary to Janssen's assertions, JanssenBr.63, Janssen's witnesses admitted **(1)** other regimens are effective, and **(2)** the reason for any "failure" of the '548 protocol was an error with its vendor that prevented Janssen from *assessing* efficacy, not that the doses would be ineffective.[5] The patent itself states that *unclaimed* regimens were safe and effective. *E.g.*, Appx170-174 (Example 8, describing regimens varying from claims at Appx170(24:3-13), and concluding all were safe and effective at Appx174(31:30-49)). Again, Janssen's hedging is telling: it says

[5] Appx10893-10897; Appx10910-10912(910:12-912:4); Appx11169(1169:2-25); Appx11359-11360(1359:9-1360:13); Appx11181-11182(1181:15-1182:24); Appx11205-11206(1205:3-1206:14).

the Phase III study underlying the '548 protocol "failed because of *inadequate* efficacy," JanssenBr.63, implying efficacy for *some* patients. Appx10893(893:4-17). Self-inflicted mistakes that led to "failed" studies (although successful for some) are not evidence of nonobviousness.

Janssen's discussion of needle length ignores or denies evidence cited in the opening brief. JanssenBr.63. Janssen included high-BMI patients in its trials. Appx11140-11141(1140:5-1141:1); Appx11144 (1144:5-12). For those patients, an intramuscular buttock injection with a 1.5-inch needle would not reach the muscle. Rather than using a longer needle, Janssen switched the injection site to the shoulder, where the 1.5-inch needle would reach the muscle. OpeningBr. 65-66. It is hardly "unexpected" that more patients reached desired blood levels when more of them actually received the medication.

b. Janssen's "industry praise" arguments repeat the district court's error of disregarding nexus. Janssen points to testimony and articles discussing benefits of long-acting injectable paliperidone palmitate *generally*. JanssenBr.63-64 (citing Appx11914-11916 (discussing rapid benefit and efficacy from LAI form); Appx20540-20543 (adherence rates are "an advantage of LAIs" administered at clinics in comparison to oral

medications filled at pharmacies); Appx20563-20569 (comparing paliperidone LAI to oral paliperidone or another drug); Appx20544-20562 (a review of studies comparing, among other things, paliperidone LAI to different drugs)).

The very prior art Janssen tries to avoid already discloses LAI paliperidone palmitate. *See, e.g.*, Appx69 n.20 ('544 patent claims and teaches "sustained-release paliperidone palmitate formulation that is therapeutically effective"); Appx70 ('548 protocol teaches injectable paliperidone palmitate doses); Appx13316-13317 (WO384's Example 4 describing "finished form" of paliperidone palmitate injections). So any praise of LAI paliperidone palmitate praises prior art, not the claimed regimen, which most physicians do not follow anyway. Appx100.

Janssen's inventors admitted the '548 protocol dosing regimens work. *See, e.g.*, Appx10893(893:4-17) (Vermeulen admitting efficacy for 100/100 mg-eq. on days 1, 8, 36, 64); Appx10863(863:1-22) (Vermeulen admitting buttock-injected 100/100 mg-eq. on days 1 and 8 better than placebo). Indeed, one article Janssen cites as "praise" actually discusses how *fixed* doses of 50 and 100 mg-eq. injected in the *buttock* on days 1, 8, and 36 showed "significant[]" improvement versus placebo. Appx20546.

It was error to rely on praise connected to prior art rather than the claims. *Geo. M. Martin Co. v. All. Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1305 (Fed. Cir. 2010).

c. Janssen cursorily defends the district court's treatment of "copying" by arguing it was not necessary to copy particle size for bioequivalence. JanssenBr.64. That ignores that even Janssen's expert admitted particle size was a result-effective variable that determines bioavailability. *See* Appx11544(1544:1-6) (particle size "controls the rate of dissolution, release and, ultimately, absorption for a formula like this"); Appx12263(2263:14-22) ("the formulation controls the release of the absorption"); *see also* Appx76 (formulation "would be controlling the rate of absorption"); JanssenBr.9 (particle size "helps ensure sustained efficacy"); JanssenBr.52. (citing its own expert testimony calling particle size and surface area "critical parameters"). Again, prior art encompassed the claimed particle size, pp.22-23, *supra*, meaning Janssen's "copying" evidence lacked nexus. *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1364 (Fed. Cir. 2012); *Iron Grip*, 392 F.3d at 1325.

d. Janssen's discussion of blocking patents, JanssenBr.60-62, repeats the district court's errors. Based on undetailed criticisms of individual experts' credibility, Jansen contends that "Teva failed to prove the *existence* of any 'blocking patents' at all." JanssenBr.60. That makes no sense. It is true that "blocking" is a "fact-specific" question, but the *existence*, term, and blocking scope of Janssen's patents were not meaningfully disputed.

Janssen listed patents in the Orange Book for Invega Sustenna and swore to the FDA that it could reasonably assert at least one claim of each patent against any generic applicant because those patents claimed either paliperidone palmitate or a method of using it. 21 U.S.C. §355(b)(1)(A)(viii); OpeningBr.70-72. Janssen thereby gained the right to stay FDA approval of any competitor's ANDA, and to keep any competitor off the market if Janssen prevailed in litigation. *E.g.*, 35 U.S.C. §271(e)(4). Janssen references 35 U.S.C. §271(e)(1)'s safe harbor, JanssenBr.61, but that only permits *development*, not sales or marketing. Even if Janssen tolerated some "development" activity, JanssenBr.61, the Hatch-Waxman Act and Patent Act empowered Janssen to prevent any actual competition from materializing.

Against that backdrop, Janssen's arguments that its product was "commercially successful" or filled a "long-felt need" are considerably weakened. Commercial success and long-felt need are not elements of a claim that are either present or absent; they are categories of evidence that shed more or less light on obviousness of the claims depending on the facts of individual cases. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

Here, it was surely relevant that the '906 patent's 2007 priority date was *fourteen years* into the term of Janssen's paliperidone palmitate compound patent. Janssen contends the '906 patent filled a "long-felt need," JanssenBr.58-59, but anyone else who tried to fill that need after *1993* would have been liable to Janssen for patent infringement.

Janssen touts the billions of dollars it has made from Invega Sustenna since 2015. But anyone else who tried to sell *any* form of paliperidone palmitate after 1993 would have been liable to Janssen, and after 2006 would have been subject to Hatch-Waxman remedies because Janssen listed the same now-expired patents for Invega ER. Janssen does not dispute these basic points. If Janssen filled a "long-felt need" in 2007 and achieved "commercial success," it is because for the previous

fourteen years *only Janssen* was permitted under the Patent Act and Hatch-Waxman Act to do so. It was error for the district court to dismiss that basic point for such irrelevancies as Teva's economic expert's partial reliance on the technical expert for the precise scope of the blocking patents. Appx112; OpeningBr.72.

If Janssen's "commercial success" is evidence of anything, it is the harm to vulnerable patients and the patent system that would result if this Court rubber-stamps the judgment. "*Net* sales" of Invega Sustenna "have exceeded $1 billion annually *every year since 2015*." JanssenBr.59. Janssen has reaped significant profits from its paliperidone patents. Other than the '906 patent, Janssen's patents covering Invega Sustenna expired in 2018. The '906 patent is Janssen's attempt to grab an extra decade of billions from schizophrenic patients, by recycling old elements. That is an abuse of the patent system, not evidence of nonobviousness.

e. Janssen's additional secondary-considerations arguments lack merit.

Janssen's long-felt-need arguments overlook the nexus requirement. JanssenBr.58-59. Janssen notes that the district court credited evidence of long-felt need for an LAI without oral supplementation and

for a larger population of patients to achieve efficacy. Appx104-105; Appx110. But as noted, the prior art already taught all the features of the paliperidone palmitate dosing regimen save "unequal" loading doses. *See ClassCo, Inc. v. Apple, Inc.*, 838 F.3d 1214, 1220 (Fed. Cir. 2016) ("A nexus may not exist where, for example, the merits of the claimed invention were readily available in the prior art" (internal quotation marks omitted)); *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991) (similar). The prior-art '548 protocol doses were successful for some patients, even with Janssen's self-inflicted errors. Appx11105-11106(1105:10-1106:9); Appx11205-11206(1205:3-1206:14).

Janssen's "skepticism" argument—which relies on the FDA's "suggest[ion]" to use lower doses, Appx97, JanssenBr.57-58—ignores the '548 protocol. That protocol, which the FDA allowed, administered back-to-back 150 mg-eq. injections in a Phase III study Janssen *expected* to succeed. Appx13244-13245; Appx11123-11124(1123:13-1124:20); Appx10758(758:6-25).

In sum, this Court need not reach secondary considerations, but if it does, that part of the district court's opinion cannot support the judgment.

II. The No-Indefiniteness Judgment for the Particle-Size Claims (19-21) Should be Reversed.

A claim is indefinite when it recites a property, but the intrinsic evidence does not convey with reasonable certainty which of multiple different measures of the property to use. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1344-45 (Fed. Cir. 2015); *Dow Chem. Co. v. Nova Chems. Corp. (Canada)*, 803 F.3d 620, 631-34 (Fed. Cir. 2015). Janssen's particle-size claims (19-21) are indefinite under that standard. OpeningBr.74-81. Janssen's response offers only misdirection.

Janssen accuses Teva of overlooking that only "significant" or "meaningful[]" differences matter. JanssenBr.65. But as Janssen acknowledges immediately afterward, Defendants indeed argued that "different methods of measuring particle size led to *materially* different results." JanssenBr.66.

Janssen contends *Takeda* "defeats Appellants' argument." JanssenBr.66. It does not. *Takeda* predates the Supreme Court's *Nautilus* and *Teva* decisions, and merely reaches Janssen's preferred result on different facts. In *Takeda*, "there was *no evidence* … that different measurement techniques in fact produced significantly different results for the same sample," and "the measurements of [the accused product]

using laser diffraction and optical microscopy, though not exactly the same, were substantially similar." 743 F.3d at 1367 (citation omitted). The opposite is true here. OpeningBr.30-31, 74-81. There was more than a "mere possibility of different results from different measurement techniques," JanssenBr.66 (quoting *Takeda*). The evidence showed that different techniques used different "equivalent sphere" models, Appx16306—thus measuring *different properties* to derive wildly different particle-size distributions. OpeningBr.78-79. The differences between Coulter and Mastersizer results were sufficiently meaningful that Janssen submitted two different specifications to the FDA, depending on whether Coulter or Mastersizer was used. Appx13179 & n.a; Appx13180 & n.a; OpeningBr.78-79.

When it turns to the evidence, Janssen ignores much of it, and denies that other evidence matters. Janssen points to nothing in the '906 patent or the intrinsic evidence that gives guidance as to *how* to determine the "particle size," recited in the claims. The '906 patent undisputedly refers only to "art-known conventional techniques," OpeningBr.76, which includes Coulter and Mastersizer. Janssen also does not dispute (or even mention) that conventional techniques use any of at least seven

different properties to derive "equivalent spheres" to estimate particle size. OpeningBr.77-78.

Faced with evidence that the Mastersizer and Coulter devices produced *materially* different results, OpeningBr.78-80, Janssen downplays the Coulter results. Janssen states it "only has 'one d50 acceptance criteria,'" and that "Janssen's material scientists resolved an apparent discrepancy between" Mastersizer and Coulter. JanssenBr.67. That is unresponsive. Janssen obtained different results for the same samples, depending on whether it used the Mastersizer or Coulter. *E.g.*, Appx20632-20633. The Coulter measurements were well outside the claims; the Mastersizer results were within the claims. Those undisputed differences led Janssen to submit two different specifications to the FDA: a lower specification if particle size was measured with Coulter, and higher if measured with Mastersizer. Appx13179 & n.a; Appx13180 & n.a.

That evidence is not "contradicted by" testimony that a different document contained "one d50 acceptance criteria." Appx10658(658:2-7, 14-17). Janssen showed, at most, that *Janssen* later came to prefer Mastersizer over Coulter. Appx10660-10662(660:20-662:17); Appx11556-

11558(1556:10-1558:9); Appx20633-20635. But Janssen's view of Mastersizer is not based on intrinsic evidence. Janssen did not show that the Coulter measurements were the result of an *individual* device malfunction, nor that Coulter was *actually* less accurate. Janssen's brief obscures this point when it refers to "an 'equipment defect' of the Coulter device," or an "instrumental 'artifact.'" JanssenBr.67-68. Janssen preferred Mastersizer only because it believed Coulter gave *systematically lower* numbers. Appx20633-20635. If a Coulter device produces a particle size outside the claimed range, is a dosing regimen using that sample noninfringing? Janssen does not say, and the intrinsic evidence gives no guidance either. This case is indistinguishable from this Court's *Dow* or *Teva* decisions, which concluded similar claims were indefinite.

CONCLUSION

The judgments should be reversed, or vacated and remanded.

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CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION

This brief complies with the type-volume limitations of the Federal Rules of Appellate Procedure and the Rules of this Court. According to the word processing system used to prepare it, the brief contains **6,903** words.

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